Studies on Leuckart-Wallach Reaction Paths

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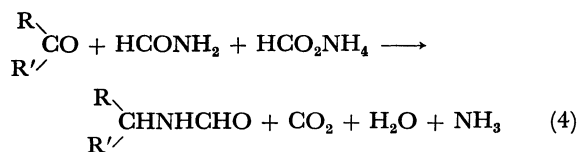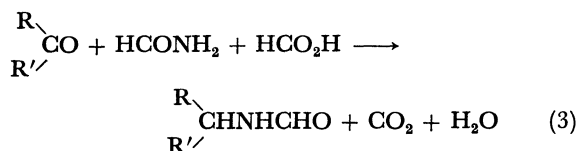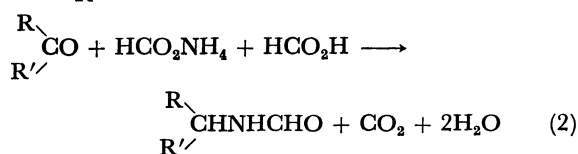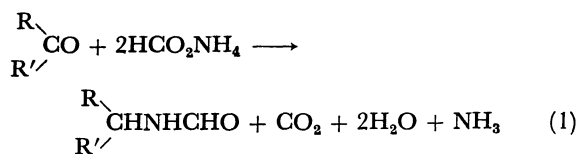*Shizuoka College of Pharmacy, Oshika, Shizuoka 422*

(Received March 17, 1975)

The Leuckart-Wallach reaction paths were investigated by means of catalytic reduction in the Leuckart-Wallach reaction system and on the basis of analogous formic acid reductions. It was determined that, in the early stage of the Leuckart-Wallach reaction, ammonia, amine and also formamide undergo addition reactions to carbonyl compounds. The addition of formamide catalyzed by formic acid plays a significant role only for the more reactive substrates such as benzaldehyde. The behaviors of plausible intermediates for the formic acid reduction are discussed on the basis of the data of similar formic acid reductions.

The Leuckart-Wallach reaction is well known[1-4] as a process for the reductive amination of aldehydes and ketones. Many workers have been involved in experiments designed to elucidate the mechanism of the reaction. Some have commented on the ammonia- or the amine-addition mechanism of the carbonyl condensation stage and others on the formamide-addition mechanism. Furthermore, the mechanism of the second stage, reduction, is still in dispute. The present work involving catalytic reduction of the Leuckart-Wallach reaction system relating to formic acid reduction bears significantly upon the understanding of the reaction path.

Results and Discussion

Process of the Leuckart-Wallach Reaction. A number of reagents such as ammonium formate, ammonium formate–formic acid, formamide–formic acid, and formamide–ammonium formate have been used[1] for reactions with carbonyl compounds. The overall reactions with respect to the formation of N-formyl primary amine can be illustrated by the equations shown in Scheme 1. The formations of N-formyl secondary amine and tertiary amine can be similarly formulated by replacing the ammonium formate and formamide with their N-alkyl analogs. The carbon dioxide formation in these reactions is indicative of the participation of formic acid as the reducing agent. Several workers have conducted the reduction of carbonyl compounds with formamide alone, although no convincing determination has been made of its reducing capacity. In these cases, the actual reducing agent may be ammonium

$$\underset{R'}{\overset{R}{>}}CO + 2HCO_2NH_4 \longrightarrow$$

$$\underset{R'}{\overset{R}{>}}CHNHCHO + CO_2 + 2H_2O + NH_3 \quad (1)$$

$$\underset{R'}{\overset{R}{>}}CO + HCO_2NH_4 + HCO_2H \longrightarrow$$

$$\underset{R'}{\overset{R}{>}}CHNHCHO + CO_2 + 2H_2O \quad (2)$$

$$\underset{R'}{\overset{R}{>}}CO + HCONH_2 + HCO_2H \longrightarrow$$

$$\underset{R'}{\overset{R}{>}}CHNHCHO + CO_2 + H_2O \quad (3)$$

$$\underset{R'}{\overset{R}{>}}CO + HCONH_2 + HCO_2NH_4 \longrightarrow$$

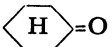$$\underset{R'}{\overset{R}{>}}CHNHCHO + CO_2 + H_2O + NH_3 \quad (4)$$

R and R': H, alkyl, or aryl

Scheme 1.

formate which can plausibly be derived from formamide by hydrolysis with water produced in the reaction mixture. In our trials of the reactions of benzaldehyde and cyclohexanone with formamide[5] (Table 1) almost no carbon dioxide was detected during the course of the reaction, which proceeded only at higher temperatures and required a much longer period. This diminishes the possibility of reduction with ammonium formate generated from formamide. In the reaction of benzal-

TABLE 1. THE LEUCKART-WALLACH REACTIONS[a] OF BENZALDEHYDE AND CYCLOHEXANONE

Run No.	Substrate	Reagent	Reaction temp (°C)	Reaction time (h)	Yield (%) of the product[b]			
					RNHCHO	R₂NCHO	R₃N	Total
1	C_6H_5CHO	$HCONH_2$	165—170	10.0	55	11	2	68[c]
2		HCO_2H–$HCONH_2$	100—105	7.7	30	8	23	61[d]
3		HCO_2NH_4	120—125	4.7	24	10	42	76
4	⟨H⟩=O	$HCONH_2$	165—170	10.0	32	30	0	62
5		HCO_2H–$HCONH_2$	110—115	6.8	30	43	0	73
6		HCO_2NH_4	100—110	4.5	21	62	0	83

a) Carried out using C_6H_5CHO (0.1 mol) and $C_6H_{10}O$ (0.2 mol) with 10-fold amounts of the reagent, $HCONH_2$, HCO_2NH_4, and $HCONH_2$ added with HCO_2H (1.5 molar equiv. to the substrate). b) Yield is based on the product isolated. $R=C_6H_5CH_2-$ and $C_6H_{11}-$. c) Amaron was obtained as a by-product. d) N,N'-Benzylidenebis-formamide was obtained as a by-product.

dehyde with formamide amaron (2,3,5,6-tetraphenyl-pyrazine), in addition to the amine products, was isolated. In previous papers by the present authors the formations of amaron and lophine (2,4,5-triphenyl-imidazole) in the reactions of N,N' benzylidenebisform-amide[6] and N-benzylideneaniline[7] with formamide are well documented and were interpreted as clues to support the idea of self oxidation-reduction reactions. In view of these papers, it is then suggested that the reaction of benzaldehyde with formamide alone appears to proceed similarly to the self oxidation-reduction course. From this abnormality of the reduction course, the reaction with formamide alone may be distinguished from others involving formic acid reduction. Accordingly, the decription hesreafter is chiefly concerned with the reactions involving formic acid reduction.

Although the Leuckart-Wallach reaction involves many elementary steps, the path of the reaction can be divided into two important stages, the formation of the C–N bond and the formic acid reduction to amine.

The Initial Condensation Stage. Two arguments have been postulated for the initial stage of the Leuckart-Wallach reaction, the addition of ammonia or amines[8-12] and the addition of formamide[12-18] to carbonyl compounds. As long as ammonium formate undergoes dehydration to formamide at the reaction temperature, the participation of ammonium formate as formamide in the reaction is possible. Conversely, the participation of formamide as ammonium formate is possible when the hydrolysis of formamide occurs

with water formed in the reaction mixture. Therefore, the interconversion[1] between ammonium formate and formamide allows the participation of these two species in every fashion of the Leuckart-Wallach reaction in Scheme 1. It has been a problem to determine whether the actual participating species is ammonium formate or formamide.

Using benzaldehyde and cyclohexanone as carbonyl compounds, preliminary experiments were undertaken on the typical reactions with formamide, formic acid-formamide, and ammonium formate (Table 1). The difficulty in defining the behaviors of the reagents comes from the dual roles played by the reagents in both the initial C–N bond formation and the succeeding reduction. In order to understand how the reagents react initially with the carbonyl compounds, it is desirable, if possible, to eliminate the succeeding reduction by the same reagents.

Experiments for this purpose were carried out on the catalytic reductions of the carbonyl compounds in the presence of the Leuckart-Wallach reagents below the temperature (100 °C) at which the reagents affect the carbon dioxide formation. In this manner, formic acid reduction is eliminated and replaced by catalytic reduction. Using a palladium-on-charcoal catalyst, high-pressure hydrogenation of the Leuckart-Wallach reaction system occurred with benzaldehyde under standardized conditions at 90—100 °C.

The affinities of formamide and N-benzylformamide for benzaldehyde can be realized from the results of

TABLE 2.[a] CATALYTIC REDUCTION[b] OF BENZALDEHYDE IN
THE LEUCKART-WALLACH REACTION SYSTEM

Run No.	Additive[c]	Reaction time (min)	Yield (%) of the product[d]					
			ROH	RNHCHO	R_2NH	R_2NCHO	R_3N	Total
a. In the system involving formamides								
1	$HCONH_2(1.0)$	120	96	0	—	0	0	96
2	$HCONH_2(1.0)$ $HCO_2H(0.5)$	160	13	28	—	20	31	92
3	$RNHCHO(1.0)$ $HCO_2H(0.5)$	80	96	97[e]	—	2	trace	98
4	$HCONH_2(1.0)$ $HCO_2H(0.5)$ $B_2O_3(1.0)$	120	62	20	—	9	6	97
5	$HCONH_2(1.0)$ $HCO_2H(0.5)$ $H_2O(1.0)$	70	38	0	—	2	52	92
b. In the system involving formates of ammonia and amines								
6	Ammonium carbonate(1.0)	30	0	0	58	—	35	94
7	$HCO_2NH_4(1.0)$	60	18	0	—	5	72	95
8	$HCO_2NH_4(1.0)$ $HCO_2H(0.5)$	40	17	0	—	5	74	96
9	$RNH_2(1.0)$	15	0	0	94	—	trace	94
10	$RNH_2(1.0)$ $HCO_2H(0.5)$	15	0	0	50	19	29	98
11	$R_2NH(1.0)$	40	25	0	24[e]	—	68	93
12	$R_2NH(1.0)$ $HCO_2H(0.5)$	30	19	0	—	20	73	92

a) $R = C_6H_5CH_2$- b) Hydrogenation condition—catalyst, 10% Pd–C, 1 g; initial hydrogen pressure, 80 kg/cm² (room temp); reaction temp, 90—100 °C. c) Molar equivalents of the additives to benzaldehyde (0.1 mol) used are given in parenthesis. d) Yield of the product isolated is calculated from the starting benzaldehyde. e) Recovery.

runs 1, 2, and 3 in Table 2, although the reduction of unreacted benzaldehyde to benzyl alcohol is shown. Formamide itself was shown to be inert to benzaldehyde. On the other hand, in the presence of formic acid, formamide led to the formation of not only N-benzylformamide but also N,N-dibenzylformamide and tribenzylamine. Under the same conditions, N-benzylformamide affected the formation of only a small amount of N,N-dibenzylformamide. In consideration of the appreciable formation of N,N-dibenzylformamide and tribenzylamine in run 2 it was then required to know whether water, which was formed in the reaction mixture, participates in the product formation, since water hydrolyzes formamide into another reactive ammonium formate. Runs 4 and 5 in Table 2 carried out in the presence of a desiccant, boron trioxide, and of water, respectively, offered clear information on the effect of water on the reaction. In the former, the addition of boron trioxide considerably reduced the yields of N,N-dibenzylformamide and tribenzylamine relative to N-benzylformamide, whereas, in the latter, the addition of water considerably increased the yield of tribenzylamine without the formation of N-benzylformamide. The result of run 5 closely resembles that of run 8 carried out using ammonium formate in place of the formamide of run 2. In view of the above facts, the water added can be understood to affect an increase in the participation of ammonium formate and the desiccant to affect an increase in the participation of formamide. In such a reaction in the presence of formic acid, the interaction between formamide and benzaldehyde is actually recognized to occur, although the participation of ammonium formate also occurs. Formic acid as an additive can then be regarded as an acid catalyst for the reaction between formamide and benzaldehyde.

Next, an examination by the same hydrogenation procedure was attempted in order to observe the behavior of ammonium formate with benzaldehyde. The catalytic reductions of benzaldehyde in the presence of ammonium formate and of ammonia (ammonium carbonate was used) resulted in the formation of tribenzylamine and dibenzylamine, in free and N-formylated forms, in the yields given in Table 2. It is inferred that dibenzylamine is derived from the initially formed benzylamine, and tribenzylamine stepwise through dibenzylamine. This was demonstrated by carrying out the reduction in the presence of benzylamine and of dibenzylamine, where the effect of the additional presence of formic acid was also checked, as can be seen for runs 9, 11, 10, and 12 in Table 2. From the above results, it was found that in the ammonium formate medium under the hydrogenation conditions, the carbonyl addition of the amine species proceeds stepwise leading to benzylamine, dibenzylamine and finally tribenzylamine. The reaction was shifted to the formation favorable to tribenzylamine when formic acid was present.

Following the same catalytic reduction procedure, an examination was then made using cyclohexanone. Formamide was, however, inert with cyclohexanone in the hydrogenation system, probably owing to the low

TABLE 3.[a]   CATALYTIC REDUCTION[b] OF CYCLOHEXANONE IN THE LEUCKART-WALLACH REACTION SYSTEM

Run No.	Additive[c]	Reaction time (min)	Yield (%) of the product[d]			
			ROH	RNH₂	R₂NH	Total
1	HCONH₂(1.0)	—	—	—	—	0
2	HCONH₂(1.0) HCO₂H(0.5)	—	—	—	—	0
3	Ammonium carbonate(1.0)	210	1	15	82	98
4	HCO₂NH₄(1.0)	210	0	6	93	99
5	RNH₂(1.0)	180	5	3[e]	92	97
6	RNH₂(1.0) HCO₂H(0.5)	180	trace	2[e]	92	92

a) $R = \langle H \rangle -$.   b) Hydrogenation condition—catalyst, 10% Pd–C, 6 g; initial hydrogen pressure, 80 kg/cm² (room temp); reaction temp, 55—60 °C.   c) Molar equivalents of the additives to the cyclohexanone (0.2 mol) used are given in parenthesis.   d) Yield of the product isolated is calculated from the starting cyclohexanone.   e) Recovery.

temperature (60 °C) which restricts the carbon dioxide formation. As can be seen in Table 3, ammonia and ammonium formate lead to the formation of cyclohexylamine and, more favorably, dicyclohexylamine. Cyclohexylamine, even in the presence of formic acid, was shown to greatly effect the formation of dicyclohexylamine in the same hydrogenation system. No formation of tricyclohexylamine from cyclohexanone was observed even for hydrogenation in the presence of dicyclohexylamine. The lack of any tricyclohexylamine formation throughout the above runs may be due to a steric hindrance.

The Formic Acid Reduction Stage.   After an understanding of the behaviors of formamide and ammonium
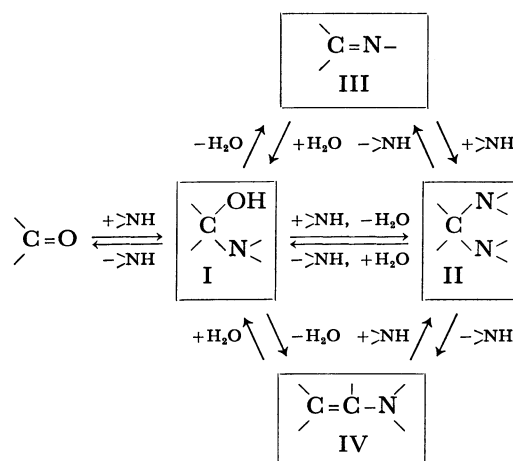

Relation to the reagent
a. In the case of $>$NH = ammonia and amines
     NH₃ and –NH₂ ⟶ I, II, III
     $>$NH ⟶ I, II, IV (with $>$CHCO–)
b. In the case of $>$NH = HCONH₂ and HCONH–
     HCONH₂ ⟶ I, II, III
     HCONH– ⟶ I

Scheme 2.

formate toward carbonyl compounds, the formic acid reduction stage in the Leuckart-Wallach reaction encounters a problem. Plausible intermediates resulting from the addition and condensation reactions of ammonia (from ammonium formate) and of formamide with the carbonyl compounds can be described as in Scheme 2. In the Leuckart-Wallach reaction, how these intermediates participate in the formic acid reduction is a subject to be studied in relation to their catalytic reductions.

For Ammonia or Amine Condensation Intermediates: Both the formic acid and the catalytic reductions of Schiff's bases[7,19] of type III and enamine[20] of type IV in Scheme 2 are well documented to result in the reduction of their C=N and C=C double bonds, respectively. In previous work,[11,21-24] several available analogs of types I and II such as

(R, R', and R″≠H) have been known to undergo reductive fission of one of the two bonds to the hetero-atom to give a tertiary amine by formic acid reduction, as well as catalytic reduction, as is shown in the following schemes:
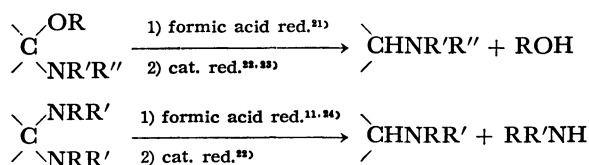
Since in these reported reduction, reductive fission has been realized to occur directly, the intermediates of types I and II

or alkyl) seem to undergo reductive fission without dehydration and deamination, respectively.

Thus, any type of intermediate shown in Scheme 2 can produce the same amine products upon reduction with formic acid, as well as upon catalytic reduction.

For Formamide Condensation Intermediates: Plausible condensation intermediates from formamide may be assumed to be of types I, II and III in Scheme 2. Previous papers appear to draw some insight relative to the formic acid and catalytic reductions of types I and II. There have been reported the catalytic reduction of 4-oxazolidinones and tetrahydro-4H-1,3-oxazin-4-ones,[25] the formic acid reduction of 3-aryl-3-hydroxy-phthalimidines[26] and the catalytic[27] and the formic acid reductions[6] of N,N'-benzylidenebisamides. These substrates are regarded as analogs of types I and II. The reductions affect the reductive fissions, as is shown by the dotted lines in the following schemes, resulting in N-acylated amines. The patterns of these reactions
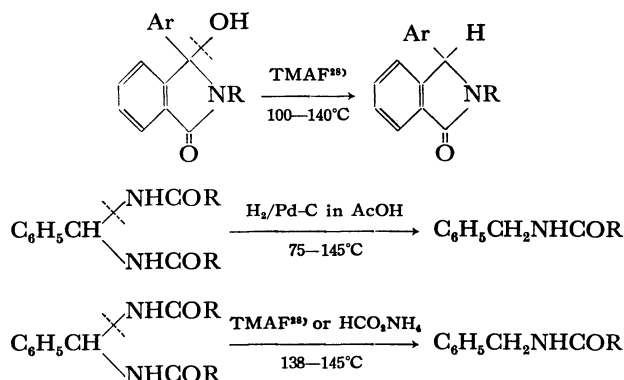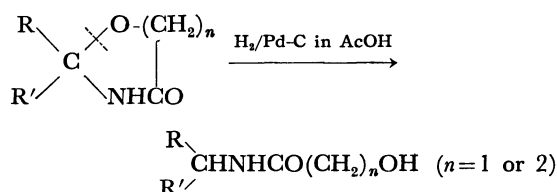
may not be in conflict in receiving types I and II as plausible intermediates.

In order to obtain further information about an intermediate of type I, an examination was directed to the synthesis of N-(α-hydroxybenzyl)amide and its formic acid reduction. The synthesis was successfully performed by the hydrolysis of N-(α-piperidinobenzyl)-benzamide with aqueous acetic acid. The formic acid reduction of N-(α-hydroxybenzyl)benzamide with TMAF[28] proceeded at 95—100 °C, while carbon dioxide was detected in a short period. Although most of the material was converted into benzaldehyde and benzamide, benzylamine was obtained even in a low yield (about 3%) through hydrolysis. Neverthless, it may be possible for the benzaldehyde reaction that N-(α-hydroxybenzyl)formamide exists in a certain equilibrium for the conventional use of a large excess of formamide. Type I is therefore referred to as a plausible intermediate in the reaction with formamide.

Comprehensive Aspect of the Leuckart-Wallach Reaction.
In spite of the confusion in the previous arguments for the Leuckart-Wallach reaction, the present work in the catalytic reduction system has demonstrated both the ammonia- or amine-addition and the formamide-addition to the carbonyl compound in the initial stage. The latter was shown to be favorable for rather reactive carbonyl compounds such as benzaldehyde, while the presence of formic acid was necessary. N-Alkylform-amide was nearly inert with the carbonyl compounds as demonstrated by the interaction of benzaldehyde with N-benzylformamide. The behaviors of plausible intermediates for formic acid reduction in the Leuckart-Wallach reaction are described in relation to their catalytic reduction which proceeded in a similar fashion giving the same amine products. Since mutual conversion between the intermediates are possible, it appears difficult to decide the actual intermediate undergoing the formic acid reduction for each of the various carbonyl compounds. In opposition to previously reported statements, clear accounts for the features of the Leuckart-Wallach reaction can be drawn from our results. In the formic acid reductions, the form-amide-condensation intermediates are reduced to N-formyl primary amine, while the ammonia- or amine-condensation intermediates are reduced to primary, secondary and tertiary amines, the former two undergoing successive N-formylation or reacting competitively with the carbonyl compound. Ammonium formate as a reacting species therefore reacts to produce tertiary

amine and/or N-formyl secondary amine rather than N-formyl primary amine, particularly under conditions accelerating the carbonyl addition (the presence of formic acid is effective), whereas formamide reacts in favor of the production of N-formyl primary amine. The reaction with formamide as given by Eq. 3, however, involves a considerable participation of ammonium formate generated from formamide by the hydrolysis with water formed in the reaction mixture. In conformity with the above features several papers dealing with the behaviors of the Leuckart-Wallach reagents for the preparative purpose of yielding N-formyl primary amine have reported that a mixture of form-amide and formic acid or ammonium formate is more efficient in several cases[9,13,16,29] rather than the use of ammonium formate alone. The predominant formation of N-formyl primary amine by the increase in the formamide participation is brought on by the reaction with formamide alone, but in this case the reduction is suggested to be caused through self oxidation-reduction of the carbonyl compound rather than by formic acid.

Experimental

Reaction of Benzaldehyde with Formamide, Formic Acid–Form-amide and Ammonium Formate (Table 1). The reactions of benzaldehyde were carried out by heating with constant stir-ring of the reagents, i.e., freshly distilled formamide (run 1), formic acid-formamide (run 2) and dried ammonium formate (run 3). The starting amounts and the reaction temperatures are listed in Table 1. In runs 2 and 3 considerable CO_2 evolu-tion was observed, whereas in the run with formamide almost none was detected even at the high temperature given. The products were concentrated by distilling off the excess of the reagents under reduced pressure in runs 1 and 2, whereas in run 3 this was accomplished by benzene extraction since the reaction mixture solidified. In run 2, N,N'-benzylidenebis-formamide, mp 148—149 °C [lit,[30] mp 149—150 °C], was isolated in a 24% yield from the residue as a benzene insoluble material. The concentrates were subjected to fractional distillation under reduced pressure to give two fractions, bp 134—136 °C/0.3 mmHg and bp 164—166 °C/0.3 mmHg, leaving a resinous residue only in run 1. The first solid frac-tion was identified as N-benzylformamide, mp 57—59 °C. The second fraction was shown to be composed of tribenzylamine and N,N-dibenzylformamide. Their separation was accom-plished by passing dry HCl through the benzene solution, resulting in the precipitation of tribenzylamine hydrochloride, mp 226—228 °C. After filtration, the filtrate was freed of HCl by treating with aqueous $NaHCO_3$, dried over $MgSO_4$ and concentrated to leave crystals which were identified as N,N-dibenzylformamide, mp 49—50 °C. The foregoing dis-tillation residue obtained in run 1 was chromatographed through silica gel using $CHCl_3$ as an eluent. From earlier fractions 1.5 g of amaron was obtained, mp 245—246 °C [lit,[30] mp 246—247 °C].

All the products obtained above were identified by compari-son of their IR spectra with those of authentic specimens and by the mixed melting point test. Their yields are shown in Table 1.

Reactions of Cyclohexanone with Formamide, Formic Acid–Form-amide and Ammonium Formate (Table 1). The reactions of cyclohexanone were carried out in a way similar to those of benzaldehyde under the conditions listed in Table 1. In the course of the reactions, considerable CO_2 was detected when

formic acid–formamide and ammonium formate were used. The reaction solutions were concentrated under reduced pres-sure to remove excess amounts of the reagents. In every run, the resulting residue was distilled into two fractions, bp 123—125 °C/4 mmHg and bp 150—154 °C/4 mmHg, leaving a resinous residue only in the run with formamide (run 4). The former fraction was shown to be N-cyclohexylformamide [Found: C, 66.36; H, 10.36; N, 10.71%. Calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01%] and the latter N,N-dicyclo-hexylformamide, mp 53—56 °C [Found: C, 74.65; H, 10.98; N, 6.71%. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.08; N, 6.69%]. Their yields are recorded in Table 1.

Catalytic Reductions of Benzaldehyde in the Leuckart-Wallach Reaction System (Table 2). In the presence of the reagents indicated in Table 2, the high-pressure hydrogenation of benzaldehyde was carried out over a Pd–C catalyst under the conditions given in Table 2. The reductions were accom-plished by constant shaking at 90—100 °C, for which a preli-minary test showed no formation of CO_2, and were continued until the pressure drop nearly ceased. After filtration of the autoclave contents, the filtrates were concentrated, whereupon benzyl alcohol was distilled together with formamide. With the addition of water to the distillates followed by distillation, benzyl alcohol alone was steam-distilled and isolated by satura-tion of the resulting distillate with K_2CO_3 and then by extrac-tion with benzene. The above concentration residues were subjected to distillation under reduced pressure. In runs 5, 7, 8, and 12, where N,N-dibenzylformamide and triben-zylamine were present in the residue, this product was distilled as a mixture at bp 142—160 °C/0.2 mmHg. Their separation was accomplished by the same procedure as described in the first section. In addition to N,N-dibenzylformamide and tribenzylamine, N-benzylformamide was present in the resi-due in runs 2, 3, and 4, and free dibenzylamine in that of run 10. For these runs all the N-benzylformamide and dibenzyl-amine were distilled separately from the other two products at bp 125—129 °C/0.2 mmHg and bp 122—127 °C/1 mmHg, respectively. In runs 6, 9, and 11, where the residue was composed of dibenzylamine and tribenzylamine, these prod-ucts were simply separated as two distillates, bp 122—127 °C/ 1 mmHg and bp 165—171 °C/1 mmHg, respectively. All the products were identified by comparison of their IR spectra with those of authentic specimens and by mixed melting point tests. Their yields are recorded in Table 2.

Catalytic Reductions of Cyclohexanone in the Leuckart-Wallach Reaction System (Table 3). As indicated in Table 3, the high-pressure hydrogenations of cyclohexanone were carried out in the presence of the Leuckart-Wallach reagents over a Pd–C catalyst. The reduction temperature was maintained at 55—60 °C, a temperature for which formic acid reduction was not effective. After filtration of the autoclave contents, the filtrates combined with methanolic rinsings were concen-trated, whereupon volatile cyclohexylamine was distilled together with MeOH. Acidification of the distillates with aqueous HCl followed by concentration gave cyclohexylamine hydrochloride. In run 4, the concentration residue was wholly solidified as crystals, while in run 6 only partly so, and the crystals were identified to be dicyclohexylammonium formate, needles from acetone–MeOH, mp 161—162 °C [lit,[15] mp 166—167 °C]. Found: C, 68.75; H, 11.08; N, 6.23%. Calcd for $C_{13}H_{25}NO_2$: C, 68.68; H, 11.08; N, 6.16%. Mix-tures composed of cyclohexanol and dicyclohexylamine were obtained as the filtrate in run 6 and as the concentration residue in runs 3 and 5. The two components of these mix-tures were separated by distillation under reduced pressure. During the distillation, dicyclohexylamine and cyclohexanol partly formed a crystalline sublimate, which was identified as

the adduct, $(\langle H \rangle-)_2NH\cdot\langle H \rangle-OH$, mp 51—54 °C [lit,[31] mp 47—48 °C]. Found: C, 76.14; H, 12.37; N, 5.02%. Calcd for $C_{18}H_{35}NO$: C, 76.80; H, 12.53; N, 4.98%. The yields of the products are recorded in Table 3.

Preparation of N-(α-Hydroxybenzyl)benzamide and its Formic Acid Reduction. A suspension of 2.9 g of powdered N-(α-piperidinobenzyl)benzamide[32] in 42 ml of 3% AcOH was heated at 85 °C for 10—15 min with vigorous stirring and then immediately cooled. The suspended precipitates were collected by filtration, washed with a small amount of cold water and quickly dried. Recrystallization from dry $CHCl_3$ gave needles of N-(α-hydroxybenzyl)benzamide, mp 100—102 °C. Yield, 0.8 g (35%). IR ν_{max} (KBr) 3265, 1640, 1520, and 1032 cm^{-1}. Found: C, 74.29; H, 5.78; N, 6.17%. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16%.

A mixture of 4.6 g of N-(α-hydroxybenzyl)benzamide and 28 g of TMAF[28] was heated with stirring at 95—100 °C for about 40 min, after which the CO_2 detected was negligible. The reaction solution was concentrated under reduced pressure, whereupon benzaldehyde was distilled off together with the excess TMAF. Basification of the distillate with KOH and extraction with benzene gave benzaldehyde in a 95% yield. In order to detect N-benzylbenzamide in the residue, which was mostly composed of benzamide, a hydrolyzed solution of the residue with 50% ethanolic KOH was subjected to GLC using a column packed with Carbowax 20 M on 20% KOH-Chromosorb W. The benzylamine was detected in a 3% yield.

References

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